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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/629,316	REDDY ET AL.	
	Examiner	Art Unit	
	Rebecca L. Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *31-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-60 are currently pending in the instant application. Claims 1-30 are rejected and claims 31-60 are withdrawn from consideration as being for non-elected subject matter.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-30 in the reply filed on 27 January 2006 is acknowledged. The traversal is on the ground(s) that there is no undue burdensome search and that the inventions are not distinct as the form I cannot be made by the same process as form III. This is not found persuasive because, in response to the burdensome search argument, the inventions are independent and distinct because there is no patentable co-action between the groups and a reference anticipating one member will not render another obvious. Each group is directed to art recognized divergent subject matter which require different searching strategies for each group. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner. In regards to the inventions of Group I and Group II being distinct, the distinctness of the groups is also shown on page 2 of the restriction requirement wherein the product of formula III can be made by another and materially different process as the products of Form III can be prepared by reacting Form I or a different potassium salt of losartan, see for example claim 31 which does not specify the form of the potassium salt of losartan and claim 53, wherein the form I of potassium losartan is used.

The requirement is therefore still deemed proper.

Claim Objections

Claims 1-9 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 38. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP 706.03(k). Each of claims 1-9 claim the crystalline Form III of losartan potassium. While claims 2-9 recite certain X-ray diffraction, DSC thermogram data, infrared spectrum data or melting range for the compound, the data recited is considered properties of the compound and are inseparable from the compound itself. Furthermore, pages 7 and 9 of the instant specification defines form III as having all of the properties as claimed in claims 1-9. Therefore, claims 1-9 are considered duplicate claims of claim 1. This objection can be overcome by deleting claims 2-9 and inserting the date from claims 2-9 into claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case, Claims 10-30 claim compositions comprising losartan potassium as a solid and pharmaceutical or veterinary compositions comprising the form III losartan potassium of claim 1.

The nature of the invention

A solid composition or a pharmaceutical or veterinary composition comprising Form III losartan potassium

The state of the prior art

The state of the prior art is that the preparation of pharmaceutical compositions requires, milling, adding excipients, surfactants, etc. The process of preparing a pharmaceutical composition will cause a specific crystalline form, if in the metastable state to resort back to the most thermodynamically stable form which is the form with the lowest vapor pressure. Polymorphs tend to convert from less stable to more stable forms (Rouhi, page 32). It is also the state of the prior art that an acceptable carrier for a pharmaceutical formulation can be water. Dissolving a specific crystalline form in water, creating an aqueous solution, would put the compound in its free form and not in a crystalline form with a specific X-ray diffraction pattern.

The predictability or lack thereof in the art

The predictability or lack thereof in the art is that a metastable compound will resort back into its most thermodynamically stable form which would have a different X-ray diffraction pattern. Also, a solution prepared from a specific crystalline form and water would contain the free form of the compound.

The amount of direction or guidance present and the presence or absence of working examples

While the specification has provided processes for the preparation of the crystalline form III, the specification does not provide examples of processes for preparing pharmaceutical compositions utilizing the crystalline form III. The specification fails to provide the steps of ensuring that the pharmaceutical compositions will maintain the specific forms as found in the specification and will not resort back to the free form or the most thermodynamically stable form of the compound.

The breadth of the claims

A solid composition or pharmaceutical or veterinary composition comprising form III losartan potassium.

The quantity of experimentation needed

The quantity of experimentation needed is undue. One of ordinary skill in the art, without direction, would be unable to maintain a specific metastable crystalline form upon preparation into a pharmaceutical composition which may require milling or formation of a solution.

The level of the skill in the art

While the level of skill in the art is high, one of skill in the art would be unable to maintain a specific metastable crystalline form upon the preparation of a pharmaceutical composition without direction and guidance which is not found in the instant specification. One of skill in the art would expect the pharmaceutical composition to contain the most thermodynamically stable form of the compound or the free form of the compound.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 6 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically claims 2, 6 and 8 refer to figures 1, 2 and 3 in the instant specification. Claims must stand alone to define the invention and incorporation into claims by express reference to specification and/or drawings is not

permitted. One must refer back to the specification to determine what applicant is claiming by referring to the figures 1, 2 and 3 of the instant specification. It is suggested that applicant insert data from figures 1, 2 and 3 into the claims.

Claims 1 and 3-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to Brittain,

> For routing work...one typically compares the powder pattern of the analyte to that of reference materials to establish polymorphic identity. Since every compound produces its own characteristic powder diffraction pattern owing the unique crystallography of its structure, powder X-ray diffraction is clearly the most powerful and fundamental tool for a specification of the polymorphic identity of the analyte. Moreover, the USP general chapter on X-ray diffraction states that the identity is established if the scattering angles of the ten strongest reflections obtained for an analyte agree to within +/- 0.20 degrees with that of the reference material, and if the relative intensities of these reflections do not vary by more than 20 percent. (see Brittain in Polymorphism in Pharmaceutical Solids, p.236).

Claims 1 and 3-9 fail to recite any X-ray diffraction peaks or recite a minimum of 5 peaks. The recitation of 5 or less peaks is not specific enough to particularly point out and distinctly claim the product that Applicant regards as his invention. The claims do not conform to the general practice in the art according to Brittain, i.e. including at least data for the 10 strongest peaks. Claims 1 and 3-9 do not contain any of the physical data that particularly points out and distinctly claims the product that Applicant regards as his invention, i.e. no claim provides at least the 10 strongest peaks of the X-ray diffraction data. For example, without this physical data, it is impossible to distinguish applicants claimed crystalline form from any other crystalline form of the prior art, since there is no data in the claims to distinguish applicants' crystalline form from any other crystalline form. It is suggested that the claims be amended to include at least 10 of the

strongest peaks of the x-ray diffraction data for form III. However additional data such as the chemical name of the compound melting temperature, DSC thermogram data and infrared spectrum data should also be included in order to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 10-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In regards to the chemical name of the losartan potassium, Form III, Form I and Form II, it is noted that while the inventor may be his/her own lexicographer, claims 1 and 10-30 do not contain any of the physical data that particularly points out and distinctly claims the product that Applicant regards as his invention, i.e. no claim provides at least the 10 strongest peaks of the X-ray diffraction data for Form I, II or III. Form I, II or III is not a limiting element and does not define a difference in the losartan potassium. Form I, II or III is not a common well recognized term in the art to define anything. While Form III is a term defined by the inventors, the definition is found in the instant specification as the XRD, melting range, infrared spectrum and DSC thermogram data. It is this data that distinguishes applicants' invention from the prior art and not the term Form III. For example, without XRD data in the claim 1, it is impossible to distinguish applicants Form III from any other crystalline losartan potassium of the prior art, since there is no data in the claims to distinguish applicants' crystalline salt from any other crystalline salt of the compound.

Prior Art Rejections

In regards to applicants compound claims 1-9, the prior art references of Breen et al. and Lo et al., while not providing applicants' instant X-ray diffraction data, do name crystalline losartan potassium which puts this product in the public domain. As these forms differ from the claims in that the references are silent on the crystalline form, applicant must show that their crystalline form really is different from any of the ones prepared in the prior art. MPEP 2112 states: "Something which is old does not become patentable upon the discovery of a new property. The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)." In this case, the "unknown property" is the particular crystalline form. This is unknown because the references are silent on this property. MPEP 2112 goes on to state: "A rejection under 35 USC 102/103 can be made when the prior art product seems to be identical except that the prior art is silent as to an inherent characteristic. Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 USC 102 and 103, expressed as a 102/103 rejection." Again, the "characteristic" which the prior art is silent on is the crystalline form.

This is not an ordinary inherency situation where it is not explicitly stated what the product actually is. Here the reference explicitly teaches exactly what the compound is. The only difference is a characteristic about which the reference happens

to be silent. Se also Ex parte Anderson, 21 USPQ 2nd 1241 and 1251, discussion of Rejection E. There, the decision states, "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." (page 1253). The "properties' branch of that statement applies here. Applicants are reminded that the PTO has no testing facilities.

The composition claims 10-30 are rejected under 35 USC 102(b) as the prior art references disclose compositions comprising applicants' instantly claimed invention as it is the state of the prior art that the preparation of pharmaceutical compositions requires, milling, adding excipients, surfactants, etc. The process of preparing a pharmaceutical composition will cause a specific crystalline form, if in the metastable state, to resort back to the most thermodynamically stable form, which is the form with the lowest vapor pressure. Polymorphs tend to convert from less stable to more stable forms (Rouhi, page 32).

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lo et al. (US Patent No. 5,130,439).

Lo et al. discloses compounds useful for the treatment of hypertension and congestive heart failure (column 1), such as the compound of example 8, 2-n-butyl-4-chloro-1[(2'-(tetrazol-5-yl)-1,1'-biphenyl-4-yl)methyl]-1H-imidazole-5-methanol, potassium salt (column 8).

Claims 1-9 and 10-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Carini et al. (US Patent No. 5,138,069).

Carini et al. discloses the compound on column 13, 2-butyl-4-chloro-1-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methyl]-5-(hydroxymethyl)imidazole, which has antihypertensive activity. See the potassium salt in Part D, column 233. Pharmaceutical compositions for the treatment of hypertension and congestive heart failure are disclosed on page 14. Columns 261-264 disclose dosage forms, capsules, tablets, soft gelatin capsules, injectable compositions and suspensions. Carriers are described on column 262 to include, for example starch. Coloring and flavoring is disclosed on column 262.

Claims 10-30 are rejected under 35 USC 102(b) as being anticipated by Campbell et al. (US Patent No. 5,608,075).

Campbell et al. discloses the forms I and II of losartan potassium, which are useful for the treatment of hypertension (column 5). See figure 2 for the x-ray diffraction pattern of Form I and Form II. Dosage forms are disclosed on columns 21-23, wherein the compositions can be administered orally in capsules, tablets and powders, or in liquid dosage forms, such as elixir syrups and suspensions. Carriers such as starch are disclosed along with coloring and flavoring to increase patient acceptance (see column 22).

Claims 1-9 are rejected under 35 USC 102(b) as being anticipated by Breen et al. (US Patent No. 5,859,258).

Breen et al. discloses losartan potassium useful for the treatment of hypertension and congestive heart failure on column 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lo et al.

Determining the scope and contents of the prior art

Lo et al. discloses compounds useful for the treatment of hypertension and congestive heart failure (column 1), such as the compound of example 8, 2-n-butyl-4-chloro-1[(2'-(tetrazol-5-yl)-1,1'-biphenyl-4-yl)methyl]-1H-imidazole-5-methanol, potassium salt (column 8).

Brittain teaches us that it is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the instant claims is that the X-ray diffraction pattern the crystalline solid of the prior art may differ from that of the X-ray diffraction pattern of the instant claims and the particle size may differ. Brittain taught that "in the strictest sense, polymorphs are different crystalline forms of the same pure substance in which the molecules have different arrangements and/or different conformations of the molecules (see Brittain p. 1-2).

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art to prepare the crystalline form as instantly claimed in claims 1-9 since the prior art reference discloses the formula of example 8. One would be motivated to prepare the instantly claimed invention because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. As it was recognized in the art that in the pharmaceutical field, many solids exhibit polymorphism which is the innate nature of the particular drug (see US Pharmacopia #23, national formulary #18). There is nothing unobvious about the innate nature of a drug. It is also recognized in the art that the innately existed different "morph" will display different physical properties such as X-ray diffraction patter, melting point etc. (see Brittian p. 178-179, 219). Just because it is "different" does not merit the new form patentability. As it was clearly stated by one having ordinary skill in the art in Brittain (p. 1-2) supra, as well as set forth by the court in In re Cofer 148 USPQ 268 and Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable. The instant specification and claims claim a known compound, which is ***the same pure substance*** as the prior art, only *having different arrangements and/or different conformations of the molecule*. Mere difference in physical property is well known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of

stability, formulation, solubility, bioavailability, ease of purification, preparation or synthesis, hydroscopicity, recovery or prevention of precipitation etc. (see p. 185).

Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline form of known compounds would have been suggested to one skilled in the art. One skilled in the art would have been motivated to prepare different crystalline forms of known pharmaceutically useful compounds with the expectation of obtaining a pharmaceutically useful benefit, such as longer shelf life, stability, enhanced deliverability, etc. Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline forms of known compounds would have been suggested to one skilled in the art. The compounds are of the same identical formula, the difference, if any, may reside in there being different crystalline forms. One of ordinary skill in the art would be motivated to prepare a different crystalline form of a known organic pharmaceutically active compound in the expectation of obtaining that very compound but with enhanced properties, e.g. improved solubility, shelf-life, improved mode of administering properties, etc. In the absence of a showing of a viable unexpected property (not just a difference in X-ray crystallography), the instant claimed invention is found obvious.

The instant claims are claiming a product which is the same pure substance as the prior art, and only has different arrangements and/or different conformations of the molecules without any disclosure of any unexpected properties. The mere differences in the physical properties are well known conventional variations for the same pure substance and are prima facie obvious over the prior art.

Claims 1-9 and are rejected under 35 U.S.C. 103(a) as being obvious over Carini et al. (US Patent No. 5,138,069).

Determining the scope and contents of the prior art

Carini et al. discloses the compound on column 13, 2-butyl-4-chloro-1-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methyl]-5-(hydroxymethyl)imidazole, which has antihypertensive activity. See the potassium salt in Part D, column 233. Pharmaceutical compositions for the treatment of hypertension and congestive heart failure are disclosed on page 14. Columns 261-264 disclose dosage forms, capsules, tablets, soft gelatin capsules, injectable compositions and suspensions. Carriers are described on column 262 to include, for example starch. Coloring and flavoring is disclosed on column 262.

Brittain teaches us that it is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the instant claims is that the X-ray diffraction pattern the crystalline solid of the prior art may differ from that of the X-ray diffraction pattern of the instant claims and the particle size may differ. Brittain taught

that "in the strictest sense, polymorphs are different crystalline forms of the same pure substance in which the molecules have different arrangements and/or different conformations of the molecules (see Brittain p. 1-2).

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art to prepare the crystalline form as instantly claimed in claims 1-9 since the prior art reference discloses the formula in part D, column 233. One would be motivated to prepare the instantly claimed invention because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. As it was recognized in the art that in the pharmaceutical field, many solids exhibit polymorphism which is the innate nature of the particular drug (see US Pharmacopia #23, national formulary #18). There is nothing unobvious about the innate nature of a drug. It is also recognized in the art that the innately existed different "morph" will display different physical properties such as X-ray diffraction patter, melting point etc. (see Brittian p. 178-179, 219). Just because it is "different" does not merit the new form patentability. As it was clearly stated by one having ordinary skill in the art in Brittain (p. 1-2) supra, as well as set forth by the court in In re Cofer 148 USPQ 268 and Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable. The instant specification and claims claim a known compound, which is ***the same pure substance*** as the prior art, only *having different arrangements and/or different conformations of the molecule*. Mere difference in physical property is well

known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavailability, ease of purification, preparation or synthesis, hydroscopicity, recovery or prevention of precipitation etc. (see p. 185).

Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline form of known compounds would have been suggested to one skilled in the art. One skilled in the art would have been motivated to prepare different crystalline forms of known pharmaceutically useful compounds with the expectation of obtaining a pharmaceutically useful benefit, such as longer shelf life, stability, enhanced deliverability, etc. Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline forms of known compounds would have been suggested to one skilled in the art. The compounds are of the same identical formula, the difference, if any, may reside in there being different crystalline forms. One of ordinary skill in the art would be motivated to prepare a different crystalline form of a known organic pharmaceutically active compound in the expectation of obtaining that very compound but with enhanced properties, e.g. improved solubility, shelf-life, improved mode of administering properties, etc. In the absence of a showing of a viable unexpected property (not just a difference in X-ray crystallography), the instant claimed invention is found obvious.

The instant claims are claiming a product which is the same pure substance as the prior art, and only has different arrangements and/or different conformations of the

molecules without any disclosure of any unexpected properties. The mere differences in the physical properties are well known conventional variations for the same pure substance and are prima facie obvious over the prior art.

Claims 1-9 and are rejected under 35 U.S.C. 103(a) as being obvious over Campbell et al. (US Patent No. 5,608,075).

Determining the scope and contents of the prior art

Campbell et al. discloses the forms I and II of losartan potassium, which are useful for the treatment of hypertension (column 5). See figure 2 for the x-ray diffraction pattern of Form I and Form II. Dosage forms are disclosed on columns 21-23, wherein the compositions can be administered orally in capsules, tablets and powders, or in liquid dosage forms, such as elixir syrups and suspensions. Carriers such as starch are disclosed along with coloring and flavoring to increase patient acceptance (see column 22).

Brittain teaches us that it is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the instant claims is that the X-ray diffraction pattern the crystalline solid of the prior art differ from that of the X-ray diffraction pattern of the instant claims and the particle size may differ. Brittain taught that "in the strictest sense, polymorphs are different crystalline forms of the same pure substance in which the molecules have different arrangements and/or different conformations of the molecules (see Brittain p. 1-2).

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art to prepare the crystalline form as instantly claimed in claims 1-9 since the prior art reference discloses the forms I and II. One would be motivated to prepare the instantly claimed invention because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. As it was recognized in the art that in the pharmaceutical field, many solids exhibit polymorphism which is the innate nature of the particular drug (see US Pharmacopia #23, national formulary #18). There is nothing unobvious about the innate nature of a drug. It is also recognized in the art that the innately existed different "morph" will display different physical properties such as X-ray diffraction patter, melting point etc. (see Brittian p. 178-179, 219). Just because it is "different" does not merit the new form patentability. As it was clearly stated by one having ordinary skill in the art in Brittain (p. 1-2) supra, as well as set forth by the court in In re Cofer 148 USPQ 268 and Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are

unpatentable. The instant specification and claims claim a known compound, which is ***the same pure substance*** as the prior art, only *having different arrangements and/or different conformations of the molecule*. Mere difference in physical property is well known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavailability, ease of purification, preparation or synthesis, hydroscopicity, recovery or prevention of precipitation etc. (see p. 185).

Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline form of known compounds would have been suggested to one skilled in the art. One skilled in the art would have been motivated to prepare different crystalline forms of known pharmaceutically useful compounds with the expectation of obtaining a pharmaceutically useful benefit, such as longer shelf life, stability, enhanced deliverability, etc. Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline forms of known compounds would have been suggested to one skilled in the art. The compounds are of the same identical formula, the difference, resides in there being different crystalline forms. One of ordinary skill in the art would be motivated to prepare a different crystalline form of a known organic pharmaceutically active compound in the expectation of obtaining that very compound but with enhanced properties, e.g. improved solubility, shelf-life, improved mode of administering properties, etc. In the absence of a showing of a viable unexpected

property (not just a difference in X-ray crystallography), the instant claimed invention is found obvious.

The instant claims are claiming a product which is the same pure substance as the prior art, and only has different arrangements and/or different conformations of the molecules without any disclosure of any unexpected properties. The mere differences in the physical properties are well known conventional variations for the same pure substance and are prima facie obvious over the prior art.

Claims 1-9 and are rejected under 35 U.S.C. 103(a) as being obvious Breen et al. (US Patent No. 5,859,258).

Determining the scope and contents of the prior art

Breen et al. discloses losartan potassium useful for the treatment of hypertension and congestive heart failure on column 1.

Brittain teaches us that it is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2).

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the instant claims is that the X-ray diffraction pattern the crystalline solid of the prior art may differ from that of the X-ray

diffraction pattern of the instant claims and the particle size may differ. Brittain taught that "in the strictest sense, polymorphs are different crystalline forms of the same pure substance in which the molecules have different arrangements and/or different conformations of the molecules (see Brittain p. 1-2).

Resolving the level of ordinary skill in the pertinent art

However, minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art to prepare the crystalline form as instantly claimed in claims 1-9 since the prior art reference discloses crystalline losartan potassium. One would be motivated to prepare the instantly claimed invention because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. As it was recognized in the art that in the pharmaceutical field, many solids exhibit polymorphism which is the innate nature of the particular drug (see US Pharmacopia #23, national formulary #18). There is nothing unobvious about the innate nature of a drug. It is also recognized in the art that the innately existed different "morph" will display different physical properties such as X-ray diffraction patter, melting point etc. (see Brittian p. 178-179, 219). Just because it is "different" does not merit the new form patentability. As it was clearly stated by one having ordinary skill in the art in Brittain (p. 1-2) supra, as well as set forth by the court in In re Cofer 148 USPQ 268 and Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable. The instant specification and claims claim a known compound, which is ***the same pure substance*** as the prior art, only *having different arrangements and/or*

different conformations of the molecule. Mere difference in physical property is well known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavailability, ease of purification, preparation or synthesis, hydroscopicity, recovery or prevention of precipitation etc. (see p. 185).

Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline form of known compounds would have been suggested to one skilled in the art. One skilled in the art would have been motivated to prepare different crystalline forms of known pharmaceutically useful compounds with the expectation of obtaining a pharmaceutically useful benefit, such as longer shelf life, stability, enhanced deliverability, etc. Therefore, absent a showing of unobvious and superior properties, the instant claimed crystalline forms of known compounds would have been suggested to one skilled in the art. The compounds are of the same identical formula, the difference, if any, may reside in there being different crystalline forms. One of ordinary skill in the art would be motivated to prepare a different crystalline form of a known organic pharmaceutically active compound in the expectation of obtaining that very compound but with enhanced properties, e.g. improved solubility, shelf-life, improved mode of administering properties, etc. In the absence of a showing of a viable unexpected property (not just a difference in X-ray crystallography), the instant claimed invention is found obvious.

The instant claims are claiming a product which is the same pure substance as the prior art, and only has different arrangements and/or different conformations of the molecules without any disclosure of any unexpected properties. The mere differences in the physical properties are well known conventional variations for the same pure substance and are prima facie obvious over the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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